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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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*Ex parte* DONALD L. WISE, DEBRA J. TRANTOLO,
DAVID D. HILE, and STEPHEN A. DOHERTY

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Appeal 2009-1867
Application 10/613,975
Technology Center 1600

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Decided: [1]July 6, 2009

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Before ERIC GRIMES, LORA M. GREEN, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] The two-month time period for filing an appeal or commencing a civil action, as provided for in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

This is a decision on the appeal from the Patent Examiner's rejections of claims 1 and 3-11. Jurisdiction for this appeal is under 35 U.S.C. § 6(b). We reverse.

## STATEMENT OF THE CASE

The claims are drawn to a vaccine composition for inducing an immune response to a pathogen. The composition comprises a "nucleic acid", such as DNA, "encoding an antigen eliciting an immune response to the pathogen." Immunization with nucleic acid coding for a pathogen antigen, rather than the antigen, itself, is an alternative way to elicit immunity in subjects. The nucleic acid is recited in the claim to be "encapsulated in a mucoadhesive controlled release particulate formulation comprising an open-celled polymeric foam of approximately 95% void volume." According to the Specification, the polymeric foam can be a poly(D,L-lactide-co-glycolide) prepared by lyophilization (Spec. 8:3-6). The Specification states that a "critical aspect . . . for inducing effective immunity in many diseases . . . is sustained and/or prolonged release [of the formulation] over a period of weeks or months, to stimulate and maintain the immune response to the pathogens" (*id.* at 8:13-16).

Claims 1 and 3-11 are pending and on appeal (App. Br. 2). The Examiner rejected the claims as follows:

1) Claims 1 and 3-11 under 35 U.S.C. § 112, second paragraph, for indefiniteness (Ans. 8);

2) Claims 1 and 3-11 under 35 U.S.C. § 112, first paragraph, for lack of enablement (Ans. 3); and

3) Claims 1 and 3-11 under 35 U.S.C. § 103(a) as obvious in view of O'Hagan (Derek T. O'Hagan, "Recent Advances in Vaccine Adjuvants for

Systemic and Mucosal Administration," 50 *J. Pharm. Pharmacol.*, 1-10 (1997)) and Mikos (U.S. Pat. No. 6,689,608, Feb. 10, 2004) (Ans. 8).

Claim 1 is representative and reads as follows:

> 1. A vaccine composition for inducing an immune response to a pathogen comprising a nucleic acid encoding an antigen eliciting an immune response to the pathogen encapsulated in a mucoadhesive controlled release particulate formulation comprising an open-celled polymeric foam of approximately 95% void volume, or particles thereof.

## INDEFINITENESS REJECTION

Claims 1 and 3-11 stand rejected by the Examiner under 35 U.S.C. § 112, second paragraph, for indefiniteness (Ans. 8). The Examiner contends that claim 1 is indefinite because it is not unclear: 1) whether it is the pathogen or the DNA, itself, which is encapsulated in the claimed particulate formulation and 2) whether the nucleic acid is from a pathogen (Ans. 8).

The claim expressly states that "a nucleic acid encoding an antigen" is "encapsulated" in the particulate formulation. Therefore, we do not agree with the Examiner, it is unclear as to whether it is the DNA ("nucleic acid") or antigen which is encapsulated.

The nucleic acid is claimed as "encoding an antigen eliciting an immune response to the pathogen." The claim language does not require that the nucleic acid be obtained from a pathogen nor does it restrict the nucleic acid's source, as long as the nucleic acid codes for an antigen which elicits "an immune response to the pathogen." The Examiner failed to identify language in the claim which would have led persons of ordinary skill in the art to a different interpretation.

The rejection of claims 1 and 3-11 as indefinite under 35 U.S.C. § 112, second paragraph, is reversed.

## ENABLEMENT REJECTION

Claims 1 and 3-11 stand rejected by the Patent Examiner under 35 U.S.C. § 112, first paragraph, for lack of enablement (Ans. 3).

### Statement of Issue

Claim 1 is to a vaccine composition for inducing an immune response to a pathogen. The composition comprises a "nucleic acid encoding an antigen" which elicits an "immune response to the pathogen." The Examiner contends that in view of the unpredictability of DNA ("nucleic acid") vaccine technology, vaccines generally, and the lack of guidance in the Specification, the claims are only enabled for the specific working examples described in the Specification (Ans. 3-4). The Examiner cited prior art publications to support the enablement rejection.

Appellants urge they do not claim to have invented DNA vaccines (App. Br. 10). They assert that the Specification provided "much evidence to show that DNA vaccines were known as of the date the application was filed" (*id.*). They state the patent application "instead" is "drawn to the advantages obtained using the [claimed] polymeric carrier" for nucleic acid vaccines (*id.*). As to the Examiner's proffered evidence, Appellants contend that the cited publications indicate that research needs to be done to *improve* efficiency of DNA vaccines, but the publications do not establish that DNA vaccines would not work (*id.* at 11).

The issue in this rejection is therefore whether Appellants have established that the Examiner erred in rejecting the claims for lack of enablement.

Principles of Law

"[T]o be enabling, the specification . . . must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application . . . ." *Id.* at 1561-1562.

"That *some* experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991) (emphasis in original).

Findings of Fact

O'Hagan

1. O'Hagan described a DNA vaccine as a vaccine "in which genes encoding antigens from pathogens are administered directly" to the subject to induce immunity (O'Hagan, at 2, col. 1).

2. O'Hagan stated that DNA vaccines were discovered in the early 1990s, but "DNA vaccination remains largely unproven in large-animal models including man, and there are significant safety concerns which need to be addressed" (O'Hagan, at 3, col. 1).

3. According to O'Hagan, "in studies performed so far in small-animal models, DNA vaccines have not out-performed alternative [existing] approaches" (O'Hagan, at 3, col. 2).

4. O'Hagan concluded: "DNA vaccines might have a significant role to play in the development of therapeutic vaccines" (O'Hagan, at 3, col. 2).

5. O'Hagan described poly(lactide-co-glycolides) as a biocompatible vaccine adjuvant to vaccine antigens for formulating vaccine microparticles (O'Hagan, at 6, cols. 1-2).

6. "Particle-size was shown to be an important factor affecting immunogenicity, because smaller microparticles (< 10 μm) were significantly more immunogenic than larger particles (> 10 μm)" (O'Hagan, at 6, col. 2).

Pachuk (Catherine J. Pachuk et al., "DNA vaccines-challenges in delivery," 2 *Current Opinion in Molecular Therapeutics* 188, 2000)

7. Pachuk states "[v]accination with DNA is a recent technology possessing distinct advantages over traditional vaccines" (Pachuk, at 188, col. 1).

8. "DNA vaccine technology, however, is still in its infancy and much research needs to be done to improve the efficiency with which these vaccines work in humans" (Pachuk, at 188, col. 1).

Watts (Allison M. Watts et al., "DNA vaccination strategies against infectious diseases," 29 *International Journal for Parasitology*, 1149-1163, 1999).

9. Watts reviews DNA vaccination strategies against infectious diseases, and includes a discussion of "systems in which DNA vaccination has

resulted in the induction of protective immunity" (Watts, Abstract). Two human clinical trials were described that "demonstrate that DNA immunisation is capable of generating and boosting the immune response to specific antigens associated with human pathogenic organisms" (Watts, at 1160, cols. 1-2).

Analysis

The Examiner bears the burden of providing an explanation as to why the full scope of the claims is not adequately enabled by the Specification. *Wright*, 999 F.2d at 1561-1562. In this case, the Examiner contends that the Specification does not provide adequate guidance "on the parameters for DNA vaccine[s] for the breadth of the claimed invention" (Ans. 4). The Examiner found that "[n]umerous factors complicate the DNA vaccine therapy art, which have not been shown to be overcome by routine experimentation" (*id.*). In addition to this, the Examiner found uncertainty in vaccine development, itself, relating to the identification of pathogen antigens that elicit immunity (*id.* at 7).

The Examiner did not meet the burden of establishing lack of enablement for the full scope of the claims. As to the DNA vaccine technology generally, we acknowledge that the technology is characterized in the prior art as being in its infancy (FF8). Yet, at the same time, it is clear that there is no barrier to its development and that immunity has been achieved in both small-animal models (FF3) and humans (FF9). While there may be room for improved efficiency (FF2, 8), the prior art indicates that the DNA vaccine technology is adequate for eliciting an immune response in animals as well as humans (FF3, 9). As the claim simply recites that the vaccine composition is "for inducing an immune response to a pathogen",

we do not interpret it to require that protective immunity be induced, as apparently understood by the Examiner.

The requirements for obtaining a patent are not the same as those for securing government approval to market a drug for human use. *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995). Therefore, while it may be accurate that human DNA vaccines are "unproven" and elicit "safety concerns" (FF2), the claims are not limited to DNA vaccines for humans nor do they require the vaccine to prevent disease, as might be necessary for a commercial vaccine and FDA approval.

Similarly, we are not persuaded that the claims lack enablement because they broadly cover pathogen antigens for eliciting an immune response (Ans. 7). It is evident from the Specification that Appellants are not claiming to have invented vaccine technology (Spec. 1:5-22), but instead are coupling existent DNA technology to a mucosal delivery system comprising a "mucoadhesive controlled release particulate formulation" (*see* Spec. 7:18-24). The Examiner cited evidence that the identification of a protein component of a pathogen is one of the key problems in vaccine development (Ans. 7), but did not establish that it would require undue experimentation to make that choice for the full scope of the claim. Rather, as argued by Appellants, suitable antigens were known in the art (App. Br. 9; Spec. 11: 14-15). The cited Ellis[2] ("*New Technologies for Making Vaccines*", 29 Vaccines, 568-575, 1988) and O'Hagan publications indicate

[2] "The development of new techniques in molecular genetics has expanded the number of approaches that can be used for making vaccines." Ellis, at 568, col. 1.

that the vaccine art was as a whole mature with many different options to choose from.

For the foregoing reasons, we reverse the enablement rejection of claims 1 and 3-11.

OBVIOUSNESS REJECTION

Claims 1 and 3-11 stand rejected by the Examiner under 35 U.S.C. § 103(a) as obvious in view of O'Hagan and Mikos (Ans. 8).

Mikos

10. Mikos describes synthetic, biocompatible, biodegradable polymeric matrices for implantation into a patient which can be vascularized by ingrowth of capillaries and connective tissue from the recipient (Miklos, at col. 4, ll. 15-21).

11. According to Mikos:

> the preferred matrix is an amorphous or semicrystalline polymer such as poly(lactic acid-glycolic acid) having a porosity (defined herein as the fraction of void volume) in the range of 50 to 95% and median pore diameter of 100 to 300 microns, more preferably a median pore size between approximately 150 and 250 microns and a porosity between 75 and 95%, which allows vascular ingrowth and the introduction of cells into the matrix without damage to the cells or patient.

(Mikos, at col. 4, ll. 46-54.)

Statement of Issue

The Examiner contends that the difference between O'Hagan and the subject matter of claim 1 is that O'Hagan does not describe nucleic acids encapsulated in "open-celled polymeric foam of approximately 95% void

volume, or a particle thereof" (Ans. 9). However, the Examiner found that Mikos taught a poly(lactic acid-glycolic acid) polymeric foam composition with a preferred void volume of between 75 and 95%, meeting the limitation of the claim (FF11; Ans. 9).

The Examiner concluded:

> One of skilled in the art would have been motivated to use polymer of 95% void volume taught by Mikos et al. replacing biodegradable polymer to deliver immunogenic compositions. One of ordinary skill in the art would have been motivated by the teachings of O'Hagan that in delivery of antigens by biodegradable polymers including PLG the particle size shown to be an important factor affecting immunigenicity [sic] (see O'Hagan page 6).

(Ans. 9.)

Appellants contend that Mikos described a foam for use in tissue regeneration, not for delivery of a nucleic acid (App. Br. 22). They argue that there would have been no motivation to have utilized Mikos's tissue regeneration foam in O'Hagan's vaccine composition (*id.*).

The issue in this rejection is therefore whether Appellants have established that the Examiner erred in combining O'Hagan with Mikos to have made the claimed invention with "an open celled polymeric foam of approximately 95% void volume."

Analysis

In rejecting claims under 35 U.S.C. § 103, the Examiner has the initial burden of presenting a prima facie case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). In this case, the Examiner recognized that O'Hagan did not describe encapsulating its DNA vaccine in "open-celled polymeric foam of approximately 95% void volume" as in claim 1, but

found this limitation obvious in the light of Mikos's teachings (Ans. 9). The Examiner's case is not supported by adequate evidence.

As argued by Appellants, Mikos's foam polymer served a different purpose than O'Hagan's adjuvant. Mikos taught that its foam have a preferred void volume of 75-95% to promote vascular and connective tissue ingrowth into it when implanted in a patient (FF10-11). O'Hagan's poly(lactide-co-glycolide) polymer, on the other hand, was described as an adjuvant to promote immunogenicity of the protein when administered to a subject (FF5-6). There was no teaching in Mikos that the preferred void volume for promoting ingrowth would also serve to promote protein immunogenicity, the purpose for which the foam was used in the O'Hagan publication. Nor did the Examiner explain why Mikos's void volume would have been understood as applicable to O'Hagan's immunogenicity problem. Accordingly, persons of ordinary skill in the art would not have considered the characteristics of Mikos's foam relevant to O'Hagan's vaccine and would not have been prompted to use it in a DNA vaccine.

The Examiner stated that the skilled worker would be motivated to utilize the void volume of Mikos because O'Hagan teaches that particle size is important consideration for immunogenicity. However, the Examiner did not provide any evidence that the particle size is related to the void volume. To the contrary, the particle size described by Mikos is 100 to 300 microns (FF11), while O'Hagan's preferred range is less than 10 microns (FF6). The Examiner did not explain why persons of ordinary skill in the art would have had reason to use the smaller sized particles in O'Hagan with the void volume of Mikos's larger sized particles.

As the Examiner did not establish prima facie obviousness, we reverse the rejection of claims 1 and 3-11 over O'Hagan and Mikos.

## SUMMARY

The rejections of claims 1 and 3-11 under § 112, first and second paragraphs and § 103 are reversed.

REVERSED

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